PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
B0045WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/09136	18/09/2000	16/09/1999
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant WARNER-LAMBERT COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22/02/2001	29.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Linker, W Telephone No. +49 89 2399 8703

Form PCT/IPEA/409 (cover sheet) (January 1994)

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09136

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-42 as originally filed

Claims, No.:

1-30 as originally filed

Drawings, sheets:

1/8-8/8 as originally filed

Sequence listing part of the description, pages:

1-102, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-30
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-30
Industrial applicability (IA)	Yes:	Claims	1-30
	No:	Claims	

2. Citations and explanations
   see separate sheet

R Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WITCHER DERRICK R ET AL: 'Characterization of the purified N-type Ca-2+ channel and the cation sensitivity of omega-conotoxin GVIA binding.' NEUROPHARMACOLOGY, vol. 32, no. 11, 1993, pages 1127-1139, XP002165606 ISSN: 0028-3908

D2: BROWN JASON P ET AL: 'Cloning and deletion mutagenesis of the alpha2delta calcium channel subunit from porcine cerebral cortex. Expression of a soluble form of the protein that retains (3H)gabapentin binding activity.' JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 39, pages 25458-25465, XP002165607 ISSN: 0021-9258

D3: BROWN JASON P ET AL: 'Isolation of the (3H)gabapentin-binding protein/alpha2delta Ca2+ channel subunit from porcine brain: Development of a radioligand binding assay for alpha2delta subunits using (3H)leucine.' ANALYTICAL BIOCHEMISTRY, vol. 255, no. 2, 15 January 1998 (1998-01- 15), pages 236-243, XP002165608 ISSN: 0003-2697 cited in the application

Document D1 discloses the use of GST fusion proteins for the purification of Ca-channel subunits, see the paragraph bridging page 1128 and 1129. This document (in combination with D2) is considered to be detrimental to the inventiveness of the subject-matter of use claims 10, 11, 15 and 16 (Article 33(3) PCT).

Document D2 discloses contacting a secreted soluble calcium channel alpha2delta subunit polypeptide with labelled gabapentin. On page 25462, right column, first paragraph, last sentence reference is made to the method of D3.

Document D3 discloses a method for screening of ligands, wherein the alpha2delta subunit is contacted with leucine and the level of binding of labelled gabapentin to the subunit is measured, see page 238 under "Radioligand Binding Assay" and Fig.2).

Therefore, the subject-matter of claims 1-9 and 20-30 appears to lack an inventive step

in view of D2 in combination with D3 (Article 33(3) PCT).

The use of a histidine tag in purification methods as such apparently is already known in the art. Therefore, claims 12-14 and 17-19 would not appear to contain any addition feature which could be regarded as inventive in view of D2.